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A CONTRIBUTION TO OUR KNOWLEDGE OF THE POLIOENCEPHALITIS SUPERIOR (WERNICKE TYPE).*

By J. RAMSAY HUNT, M. D.,

NEW YORK,

CHIEF OF THE CLINIC FOR NERVOUS DISEASES AND INSTRUCTOR IN NERVOUS DISEASES IN THE CORNELL UNIVERSITY MEDICAL COLLEGE.

(From the Pathological Laboratory of the Cornell University Medical College.)

In the year 1881, Wernicke, on the basis of three cases, described a clinical picture running a very acute course, characterized by the development of associated ocular palsies, a staggering gait, optic neuritis and an agitated delirium, similar to delirium tremens. Ptosis was absent in these cases and the intrinsic muscles of the eyes were spared; all terminated fatally in from 10 to 14 days. Alcoholism was regarded as the chief ætiological factor. Post mortem a hæmorrhagic inflammation limited to the central gray matter of the third and fourth ventricles and aqueduct of Sylvius was found, and the affection was called "Polioencephalitis acuta hæmorrhagica superior."

The syndrome as originally depicted by Wernicke, while still retaining its general and very characteristic features, has undergone certain changes and modifications. Subsequent observations show that the levator palpebræ superioris is not always spared, and ptosis often only partial has occurred in one half the cases. The intrinsic muscles of the

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eye are also rarely involved. Paralysis of the extremities may result from invasion of the white matter and the inflammatory process may extend to the medulla and spinal cord, constituting the so called polioencephalitis superior et inferior and the polioencephalomyelitis.

As in other forms of encephalitis, so here the termination is by no means always fatal, and many instances of complete or partial recovery are recorded. It is important to recognize these partial recoveries with their residual ocular and locomotor symptoms which might otherwise give rise to diagnostic error and confusion. The pathological anatomy of the affection has remained fundamentally the same. It is an encephalitis with a marked hæmorrhagic tendency, displaying a predilection for the central gray matter, but by no means always limited to this distribution, as described by Wernicke and the earlier observers. The white matter of the medulla and the pons is frequently involved, and in a few cases the basal ganglia and the cerebral hemispheres have shown extensive areas of encephalitis.

In a personal analysis of 23 cases with post mortem studies, the hæmorrhages and foci of encephalitis were confined to the central gray matter in 15. (In some of them the microscopical examination was incomplete.) In eight cases the white matter showed more or less extensive invasion. This latter group of cases, with disseminated lesions in both white and gray matter, form a pathological bond of union between the polioencephalitis of the Wernicke type, the so called Strümpell-Lichtenstern type and encephalitis in general.

The poliœncephalitis superior also presents transition forms to another group of cases in which the insignificant lesions found do not explain adequately the symptoms observed during life. Oppenheim and Patrick have described cases of this character which they interpret as obscure toxic states stand-

ing midway between inflammatory affections of the central gray axis and the asthenic bulbar palsy without anatomical findings. These cases are so few in number and so obscure that any generalization is impossible. They suggest, however, the possibility of selective nuclear palsies of toxic origin.

The chief interest of the case here recorded, quite typical clinically, is in the nature of the pathological findings. The evidences of hæmorrhagic encephalitis while unmistakably present are comparatively slight in degree, suggesting the action of a toxic agent in the production of symptoms. Furthermore the areas of encephalitis, while confined to the brain stem, are equally distributed in both the gray and white matter, thus stamping the case as a disseminated hæmorrhagic encephalitis as contrasted with a pure polioencephalitis.

(From the Cornell Medical Division of Bellevue Hospital, service of Dr. H. P. Loomis.)

Summary of Case: The patient is a man, aged 40 years, with excessive indulgence in alcohol for many years. Sudden onset after an alcoholic debauch with headaches and vomiting followed by diplopia and partial ptosis. Somnolence alternating with periods of great restlessness. Incoherent delirium. Complete external ophthalmoplegia on both sides sparing the sixth nerves. Pupils are unequal, but react. Later bradycardia, irregular respirations, moderate fever, and palsies of the soft palate. Death in coma from respiratory failure. Duration of illness, five days.

Clinical Diagnosis: Polioencephalitis acuta superior.

Autopsy: Pachymeningitis interna hæmorrhagica unilateralis, with fresh hæmorrhages into the subdural space. Œdema of the brain, disseminated minute hæmorrhagic foci, perivascular hæmorrhages and small scattered foci of encephalitis, equally distributed over the gray and white matter of the medulla and pons. The cerebellum, cerebral hemispheres, and basal ganglia show no evidence of encephalitis.

History of Case: The patient was born in Ire-

land, is forty years of age, family history negative. He had gonorrhœa at eighteen and a chancre with secondary manifestations at twenty-three. With the exception of the infectious diseases of childhood, his only illnesses have been diphtheria at 20 and malaria at 36. For many years his livelihood has been gained doing general work in restaurants and kitchens, affording him unusual opportunities for excessive indulgence in alcohol. He has averaged for some years from ten to fifteen beers and several whiskeys every day, besides numerous debauches. Just before the onset of the present illness he had been drinking hard. On Wednesday, October 26, 1904, he awoke in the morning with a severe headache and feeling very tired and languid. He worked all that day and the next, but on Friday, October 28th, the headaches were so severe and the prostration so great that he remained in bed. The headaches continued Friday and Saturday with great intensity, and were accompanied by vomiting. Sunday, October 30th, he walked to Bellevue Hospital accompanied by a friend, and was admitted to the Cornell Medical Division, in the service of Dr. H. P. Loomis. On admission he complained bitterly of headaches, more especially on the right side, vomiting, and great general weakness. It was noticed at this time that the eyelids drooped slightly on both sides, more on the right, and diplopia was present. The pupillary reactions were normal. The gait and station showed only a general weakness. The tendon reflexes were exaggerated. The urine was free from albumin or sugar; examination of the thoracic and abdominal organs was negative. Mentally the patient was dull and somewhat confused, but responded correctly to all questions. As night approached he became restless and delirious, the temperature reached 100° F., pulse 64, respirations 26.

On October 31st the dulness and apathy has increased; patient is somnolent and at times almost stuporous. He can be aroused, however, and answers questions distinctly and correctly. The ptosis is now marked on the right side and has increased on the left. The pupils are unequal, the left is the larger, and is irregular in outline. Reactions to light and in accom-

modation are present, but sluggish. All of the extrinsic muscles of both eyes are paralyzed with the exception of the external recti, and a very slight inward rotation of the right internal rectus. He can stand and walk, but is very weak and staggers. The Babinsky reflex is present on both sides. The temperature ranges from 99° F. to 100° F., pulse 50, respiration 20. During the night delirium and great restlessness is prevalent, the patient continually getting out of bed.

November 1, 1904. Periods of somnolence alternating with great restlessness and low muttering delirium. He tosses from side to side, arms and legs are in constant movement, clawing the air, picking at the bed clothes. Restraint is necessary. Periods of stupor with irregular stertorous respirations. Hutchinson's face is well marked; the ptosis is complete on the right and almost complete on the left. The sixth nerves are still intact, the only other movement of the eyeballs present is a slight inward rotation of the right eye. The pupils are unequal, moderately contracted and react sluggishly. The gross motor power of the extremities is well preserved; the tendon reflexes at the knee and ankle are exaggerated. A coarse tremor is present in both upper extremities. There is pseudo-ankle clonus on the left, which is not elicitable on the right, owing to an old ankylosis (osteomyelitis with operation). The abdominal and cremasteric reflexes are present and the Babinsky reflex is elicitable on both sides. Reacts promptly to pain stimuli on the trunk and extremities. Professor Dana examined the patient at this time and confirmed the clinical diagnosis of polioencephalitis acuta superior. To-day was noted for the first time a difficulty in swallowing, with choking and regurgitation after taking liquids. A paresis of the soft palate is quite apparent on voluntary innervation. The fifth, sixth, seventh, and twelfth cranial nerves are unaffected. There is no gross defect of sight or hearing, finer ophthalmological tests are impossible. The outline of the left disc is clear and distinct, the veins distended, no optic neuritis. The right disc could not be seen. Incontinence of urine and fæces. Temperature rises from 98° F. to 100° F. Pulse rate is 44, 54, 56, and 64 during the day, and

full and soft; respirations 18. Patient passes into a comatose state, dying quietly at 12.45 a. m. of respiratory failure.

AUTOPSY: Pathological diagnosis: Polioencephalitis acuta superior, pachymeningitis interna hæmorrhagica, chronic apical tuberculosis (healed); chronic interstitial nephritis; chronic splenitis and perisplenitis.

The post mortem examination was made by Dr. Charles Norris, pathologist to Bellevue Hospital, fifty-seven hours after death. His notes read as follows:

Rigor mortis has disappeared. Ribs are ossified. Heart: Pulmonary and tricuspid valves normal, likewise mitral and aortic valves. No atheroma of the aorta or coronary arteries. Lungs: A few adhesions at the apex of the right lung posteriorly. Firm adhesions over the upper left lobe; bronchi contain some mucous pus, and are slightly reddened; lungs are posteriorly œdematous; the upper lobe of the right lung is firm and on cross section is smooth; it contains whitish raised areas the size of a pinhead; the upper lobe of the left lung presents the same condition as the right; the lower lobes are reddish and dry; bronchial lymph glands are anthracotic and show no tubercles. Liver: Normal. Somewhat pale on cross section. The suprarenals are normal. Kidneys: Firm, surface granular, and the capsule adherent in places; cortex is thin and markings indistinct. The lymph nodes of mesentery are normal. Stomach and intestines are normal. The spleen is firm, capsule thickened. Brain: The dura mater is not adherent; on turning it back the under surface on the right side is found to be the seat of an extensive pachymeningitis interna hæmorrhagica, with large fresh hæmorrhages which have visibly compressed the Rolandic area. Fresh blood clots are also found in the anterior, middle and posterior fossæ of the skull on the right side, having filtered down from the cortex. The dura mater on the left side is free from any gross changes, but on very careful inspection there is visible in certain areas a very fine and delicate rusty membrane. There is no laceration of the cerebral cortex and no subpial extravasation of blood. No evidence of fracture of the skull, although the dura was carefully stripped from

both, calcarium and the base of the skull. The vessels of the circle of Willis are normal. The ventricles of the brain contain a moderate amount of clear fluid. The ependyma is normal. Brain stem: After removal of the cerebral hemispheres and the cerebellum, the medulla, pons, and basal ganglia were divided at close intervals by a systematic series of transverse cuts. The puncta vasculosa are prominent, especially in the pons Varolii, which is also soft and moist to the touch. The œdema is not so apparent in the medulla and basal ganglia. In the pons a few minute red spots appear to indicate an actual hæmorrhage, but these are small and few in number. No hæmorrhagic foci were observed in the gray or white matter of the cerebral cortex, cerebellum, or basal ganglia. From the naked eye examination alone the existence of hæmorrhagic encephalitis could not have been determined with certainty.

Microscopical Examination: Tissues were fixed in ten per cent. formalin. Alternate levels of the medulla, including the first cervical segment, the pons and basal ganglia as far forward as the anterior commissure, were treated by me by the following methods: Nissl, Marchi, Weigert-Pal with counterstain, hæmatoxylin and eosin, Van Giesen. Large areas from the frontal and parietal lobes and cerebellum were studied by the Nissl, hæmatoxylin, and Van Giesen methods.

The result of this examination is as follows: The leptomeninges enveloping the brain stem are free from any inflammatory changes, save a few isolated collections of round cells between the layers of the pia and in the perivascular spaces at the glossopharyngeal level of the medulla. These changes are only very moderate in degree, and are present only at this level. The meningeal bloodvessels show considerable thickening throughout, especially of the media, and many of the central arteries of the pons and medulla are sclerosed and the lumen narrowed. At the level of the glossopharyngeal vagus and immediately above the nucleus ambiguus, a small focus of inflammation is present on both sides. There is perivascular infiltration of round cells and several small aggregations of mononuclear leucocytes are found scattered in the surrounding tissues. These inflammatory changes while symmetrical are more intense on one side.

At the level of the abducens nucleus a single large vessel in the gray matter of the floor of the fourth ventricle is enormously distended with blood and traced in a series of sections, it is found to have ruptured with a small extravasation of blood into the surrounding tissues. At this same level a few vessels contain perivascular accumulations of round cells. At the levels of the trigeminus, trochlearis, and motor oculi nuclei, a few of the vessels are greatly distended with blood, some with perivascular hæmorrhages or rupture and moderate infiltration of the neighboring parts with blood cells. A few of the hæmorrhagic foci are equal in size to a grain of wheat, but the average size is from one half to one third smaller, and many are microscopic. They are not numerous, not more than four or five foci are to be found in any one section of the pons. On the whole, they are rather less frequent in the gray matter surrounding the aqueduct than in other regions. At the level of the third nerve and in immediate juxtaposition to the anterior of the oculomotor nucleus on one side one vessel only has ruptured with a small extravasation of blood, although several vessels nearby are greatly distended with blood and contain blood in the perivascular sheath. Many of the smaller vessels of the medulla and pons are greatly distended with blood, others again are of normal calibre, containing only a few corpuscles.

The neural structures of the pons and medulla, especially in the neighborhood of the hæmorrhages, appear rarefied, with well marked interstices suggesting an œdematous condition. The perivascular lymph spaces are very generally dilated, some containing a fine granular deposit. In the pons a few small aggregations of round cells are detected and an occasional vessel with perivascular accumulations of round cells, but no large or well defined area of encephalitis was discerned. In the basal ganglia adjacent to the third ventricle, as far forward as the anterior commissure, no hæmorrhages, round cell infiltration, or other indications of encephalitis could be found. The sections taken from the frontal and parietal lobes and cerebellum were likewise negative. The Marchi preparations of the medulla, pons, and tweenbrain showed no de-

generations and no fat granule cells. Sections treated by the Nissl method included the first cervical segment and the nuclei of the twelfth glossopharyngeal vagus and trochlearis nerves. The cells comprising these nuclei were normal in outline, with normal processes and a centrally situated nucleus. The increased chromatophilia of the nucleus and clumping of the Nissl granules must be attributed to post mortem changes. Similar changes were observed in the cells of the cerebral cortex and cerebellum which were otherwise normal.

Dura mater. The neomembrane attached to the inner surface of the dura mater is very vascular and contains within its meshes round cells filled with blood pigment and the débris of red cells. These cells are swollen and are relatively rich in protoplasm. Extravasations of red blood cells and hæmorrhages are freely distributed between the layers of the membrane.

Remarks.—In its clinical features the case deviates but little from the usual type. The excessive alcoholism and acute onset following a debauch; the associated ocular palsies; the somnolence alternating with delirium; the staggering gait and fatal termination in four or five days, constitute a characteristic clinical picture. The development of bulbar symptoms, however, is somewhat rare, and would classify the case with the polioencephalitis superior et inferior group. The chief interest centers in the nature and distribution of the pathological findings. The recognized histological changes described in this affection were present but in a mild degree. The only well marked foci of encephalitis were found in the medulla at the glossopharyngeal level.

A considerable number of vessels, however, throughout the pons and medulla contain accumulations of round cells in the perivascular lymph spaces, also small isolated groups of round cells are here and there demonstrable. The hæmorrhagic extravasations are slight and few in number and are confined to the pons Varolii. I would particularly

emphasize the equal distribution of these lesions in both the gray and white matter. The case therefore while clinically a polioencephalitis of the Wernicke type has pathologically the lesions by no means limited to or even predominant in the gray matter. It is properly speaking a disseminated hæmorrhagic encephalitis of the pons and medulla. Interesting is the selective action of the intoxication on these structures alone. The pachymeningitis interna hæmorrhagica has been found associated with acute polioencephalitis in two other cases, those of Eisenlohr and Zingerle. Its relation to chronic alcoholism is well known and its presence in this group of cases is not surprising.

It would be difficult to say in what manner the unilateral pachymeningitis with hæmorrhages may have affected the clinical picture in my case. It may be said that while a large cortical blood clot was present at autopsy, visibly compressing the subjacent brain substance, some of which had gravitated into the fossæ of the skull, the patient had at no time had a convulsive seizure, nor was a hemiplegia demonstrable before the advent of coma.

Bibliography.

(Cases of polioencephalitis superior acuta with autopsy.)

Boedeker. *Archiv für Psychiatrie,* 1895, vol. xxvii.

Brissaud et Brecy. *Revue de neurologie,* 1904, p. 899.

Church. *Journal of Nervous and Mental Disease,* 1901, p. 303.

Eisenlohr. *Deutsche Zeitschrift für Nervenkrankheiten,* 1899; *Deutsche medizinische Wochenschrift,* 1892, No. 47.

Goldscheider. *Charité Annalen,* vol. xvii.

Hamilton. *Journal of Medical Research,* 1902, p. 11.

Hori and Schlesinger. *Obersteiner's Arbeiten,* vol. iv, p. 263.

Jacobaeus. *Deutsche Zeitschrift für Nervenkrankheiten,* 1894. vol. v.

Köppen. *Archives of Psychiatry,* vol. xxx.

Koshewnikoff. *Progres médical,* 1887, No. 36 and No. 37.

Luce. *Neurologisches Centralblatt,* 1903, p. 380.

Oppenheim. *Deutsche Zeitschrift für Nervenkrankheiten,* 1899, vi. *Archiv für Psychiatrie,* 1892, No. 10, p. 595.

Patrick. *Journal of Nervous and Mental Disease,* 1897.
Rainmann. *Neurologisches Centralblatt,* 1902, p. 976.
Rennert. *Deutsches Archiv für klinische Medizin,* vol. i, 1892.
Schüle. *Archiv für Psychiatrie,* vol. xxvii, p. 295.
Spielmayer. *Neurologischer Centralblatt,* 1904, No. 23, p. 1126.
Thomson. *Archiv für Psychiatrie,* 1888, vol. xix, p. 185.
Wernicke. *Lehrbuch,* vol. ii, p. 229.
Wilbrandt and Saenger, vol. i, p. 270.
Wijinhoff and Scheffer. *Jahresbericht für Neurologie und Psychiatrie,* 1900, p. 443.
Wijinhoff and Scheffer. *Jahresbericht für Neurologie* vol. ii, p. 137.

102 East Thirty-seventh Street.